Analysis of Acid Fraction. Method D.—A modification of the procedure of Metcalfe and Schmitz[14] was used. A 0.1- to 5.0-g. sample of acid was refluxed on the steam bath for 1 hr. with a 10–15-fold weight excess of BF_3–methanol reagent (125 g. of BF_3 in 1 l. of dry methanol). At the end of this period, the condenser was disconnected and the bulk of the volatile solvent was allowed to boil away (15–20 min.). The concentrate was diluted with methylene chloride and extracted with water and then saturated sodium bicarbonate solutions. If a precipitate occurred when the latter was acidified, the conversion to ester was incomplete and a quantitative determination could not be made.

After removal of the solvent, the methyl esters were separated and analyzed with a vapor phase chromatograph utilizing a 0.25-in., 20-ft. aluminum column packed with 5% SE-30 silicone oil on 60–80-mesh Chromosorb W. Helium was used as the carrier gas at a flow rate of 300 cc./min. The various components were trapped as they emerged and identified by a comparison of their infrared spectra with those of authentic samples. Known mixtures of acid were used to determine the relation between the peak area and mole fraction of the various components. A representative comparison of results obtained with methods C and D is shown in Table III.

Isolation of Pure Salicylic Acids. Method E.—A countercurrent extraction method has been described.[2] The salicylic acid forms a highly colored complex with aqueous ferric chloride from which the corresponding starting benzoic acid derivative can be extracted with methylene chloride. The stability or water solubility of this complex, and consequently the success of the separation technique, varied considerably with the various ring substituents on the salicylic acid. Strong electron-withdrawing groups appeared to weaken the complex. Hydrophobic groups, such as *t*-butyl, appeared to reduce the water solubility of the salicylic acid complex. As a result, larger volumes of the aqueous phase were used. It was also discovered that the aqueous complex could be decomposed with acid. This greatly facilitated the final isolation of product.

TABLE III

	% salicylic acid	
Run no.	Method C	Method D
2[a]	69.5	69.6
3[a]	73.7	73.1
3[b]	10.4	10.2
8[a]	29.2	30.8

[a] Acids isolated from the ether-insoluble Cu(I) salt fraction. [b] Acids isolated from the ether-soluble fraction.

To specifically illustrate the improved method, the work-up of run 17 will be described. A 7.5-g. sample of the mixture of acids obtained from the decomposition of the insoluble cuprous salts was dissolved in 400 ml. of methylene chloride. This was agitated with 1500 ml. of 0.33 *M* aqueous $FeCl_3$ solution. After separation of the organic phase, the purple-black aqueous complex was extracted with three 250-ml. portions of methylene chloride, filtered, and made acid with gaseous HCl. The purple color was replaced by the characteristic orange color of the ferric chloride. After cooling to room temperature, fine needles of *p*-methoxysalicylic acid separated. The slurry was extracted with methylene chloride to give 2.2 g. of the product, m.p. 160° after recrystallization from water. A second extraction of the methylene chloride phases, reduced in volume to 400 ml., in a similar manner, gave 1.21 g. of product. The identity of all of the salicylic acid derivatives was established by a comparison of the physical properties or infrared spectra with those of authentic samples.

Acknowledgment.—We are indebted to Mrs. Veda M. Brink for assistance with the experimental work, Mr. H. O. Kerlinger for advice and help with the analytical problems, and Mr. M. D. Yeaman for assistance with the interpretation of the X-ray diffraction patterns.

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(14) L. D. Metcalfe and A. A. Schmitz, *Anal. Chem.*, **33**, 363 (1961).

Oxidation of Aromatic Acids. VI. Reaction of Cupric Salts of Carboxylic Acids with Aromatic Aprotic Compounds

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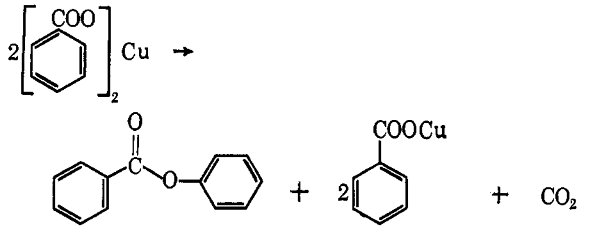
Cupric salts of carboxylic acids have been used to oxidize a variety of aprotic aromatic compounds. Ring hydrogen atoms were replaced by the acyloxy group of the salt $[2(RCOO)_2Cu + R'C_6H_5 \rightarrow R'C_6H_4OCOR + 2RCOOCu + RCOOH]$. The ratios of isomers produced with a variety of monosubstituted benzene derivatives was approximately 1:2:1 for *ortho–meta–para* positions, respectively. The proposed mechanism is discussed in terms of single-electron transfers by a pair of cupric ions.

When cupric benzoate is heated with a variety of aprotic, aromatic compounds, a two-electron oxidation–reduction reaction occurs. The electrons are transferred to a pair of cupric ions which are converted to the cuprous form. The aromatic compound is oxidized by the replacement of a ring hydrogen atom with the acyloxy group of the salt.

There are two different aromatic compounds in this system, the benzoate ion of the copper salt and the aromatic substrate (solvent). Each competes for the oxidizing power of cupric ion. Since distinctive compounds are usually produced, the relative amount of reaction by each path may be determined by an analysis of the reaction products.

Only one aromatic species is present where benzoic acid is used as the solvent. The product of reaction in this case is phenyl benzoate[2] (eq. 1). A simple



(1)

hydrolysis will liberate the phenol. This reaction provides the basis for a commercial process for the production of phenol from toluene *via* benzoic acid,[3,4] and will be referred to as the *phenol reaction*.

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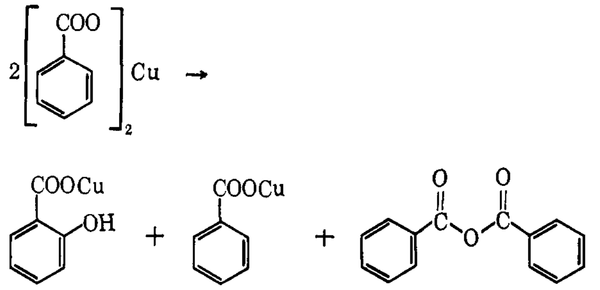
[1] To whom inquiries should be sent: Mobil Chemical Co., Metuchen, N. J.

(2) W. W. Kaeding, *J. Org. Chem.*, **26**, 3144 (1961).

(3) W. W. Kaeding, R. O. Lindblom, and R. G. Temple, *Ind. Eng. Chem.*, **53**, 805 (1961).

(4) W. W. Kaeding, R. O. Lindblom, R. G. Temple, and H. I. Mahon, *Ind. Eng. Chem., Process Design Develop.*, **4**, 97 (1965).

In the previous paper of this series,[5] it was shown that phenyl benzoate is produced by the decarboxylation of *o*-benzoyloxybenzoic acid, the primary intramolecular oxidation product of cupric benzoate. This was the predominant reaction when a protic solvent (benzoic acid) was used.[2] When aprotic solvents were used, however, the decarboxylation reaction was repressed.[5,6] The *o*-benzoyloxybenzoic acid intermediate was converted to salicylic acid by a reaction with free benzoic acid liberated during the other primary step (eq. 3). The over-all reaction for the production of salicylic acid from cupric benzoate by this intramolecular path is shown by eq. 2, and it will be referred to as the *salicylic reaction.*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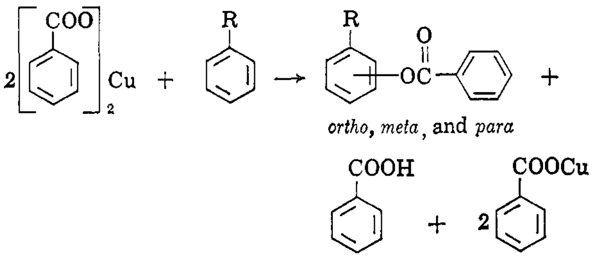
The cupric benzoate can also react with an aprotic aromatic substrate (solvent) by an intermolecular path to give an ester. This will be referred to as the *ester reaction*, eq. 3, to distinguish it from the other competing reactions.



(3)

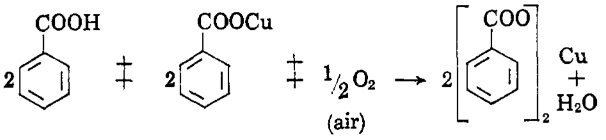
Results

Cupric benzoate was heated with a variety of aprotic aromatic compounds. The conditions of reaction and the products recovered are summarized in Table I.

The distribution of the oxidizing power of the cupric ion between the three reactions under discussion may be calculated. With toluene, for example (run 6), the results are salicylic reaction, 33%; phenol reaction, 16%; and ester reaction, 51%. In a similar manner, it can be shown that a little less than half of the oxidizing power of the cupric ion is used for the ester reaction, with a variety of mono- and disubstituted benzene derivatives.

The quantity of oxidizing power possessed by the original charge of cupric salt was relatively small. A higher degree of conversion to products was accomplished by the addition of cupric oxide. For example, an average of 6.1 mmoles of oxidation products was obtained from 16.4 mmoles of cupric ion with runs 1–3. With runs 4 and 5, where the only change was the addition of 49 and 69 mmoles of cupric oxide, respectively, 11.3 and 12.8 mmoles of oxidized product were produced. The benzoic acid liberated by the ester reaction, eq. 2, reacted with the oxide to produce more cupric benzoate and water. The latter produced more free benzoic acid from benzoic anhydride, eq. 3. The significant over-all effect was the generation of a substantial amount of cupric benzoate.

An alternative procedure to increase the conversion to products utilized air for the regeneration of cupric benzoate, eq. 4. This reaction proceeds with ease and is a vital component of the commercial process for the oxidation of benzoic acid to phenol.[3,4] The net result of (3) and (4), eq. 5, indicates that air may be used in the presence of catalytic amounts of copper. With run 19, for example, where air was bubbled through the reaction mixture, 1.27 moles of oxidized products was obtained starting with 1.02 equiv. of cupric ion. With run 1, where air was not present, 5.8 mmoles of oxidized product was obtained from 8.2 mequiv. of cupric ion.



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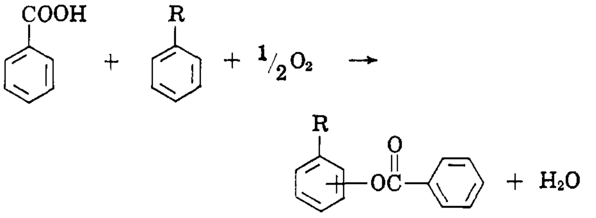
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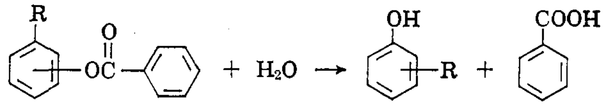
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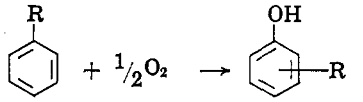
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Hydrolysis of the product produced by the ester reaction, eq. 6, will release the corresponding phenol. A summary of the entire sequence of reactions, eq. 7, presents a new general method for the production of phenols from aprotic aromatic compounds by oxidation with air, in the presence of catalytic amounts of copper salts and water. A higher degree of conversion is assumed when the air is bubbled through the reactor for long periods of time.

From a practical point of view, a suitable choice of reaction conditions will cause any one of these reactions to be dominant. When aliphatic hydrocarbon substrates are used, the ester reaction is suppressed. With cyclohexane, the distribution was 11% phenol reaction and 89% salicylic reaction (run 9).

The phenol reaction occurs when the intermediate *o*-benzoyloxybenzoic acid undergoes a decarboxylation reaction.[6] This is the dominant path when protic solvents such as water or benzoic acid are used.[5]

The cyclic mechanism proposed for the phenol[2] and salicylic[6] reactions, eq. 8, suggests that the products are derived from the aromatic carboxylate anion of the copper(II) salt. If the copper salt of an *ali-*

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(5) W. W. Kaeding and G. R. Collins, *J. Org. Chem.*, **30**, 3750 (1965).

(6) W. W. Kaeding, *ibid.*, **29**, 2556 (1964).

TABLE I

REACTION OF CUPRIC BENZOATE WITH AROMATIC COMPOUNDS

Run no.	Reactants, mmoles		Reaction conditions		Compounds recovered, mmoles											Material balance, aromatic rings out/in, %
					Salicylic reaction				Phenol reaction	Ester reaction						
										$C_6H_5COOC_6H_4R$				$C_6H_5COOCH_2C_6H_4R'$		
	Cupric benzoate	Aromatic compd.[a]	Temp., °C.	Time, min.	o-HOC_6H_4-COOH	o-HOOC-C_6H_4O-COC_6H_5	$(C_6H_5CO)_2O$	C_6H_5COOH	C_6H_5-$COOC_6H_5$	R	*ortho*	*meta*	*para*	R'		
1	16.36	Benzene	250	15	2.12	0.55	3.42	19.24	3.16[b]	...	...	...	...	...	...	99
2	16.36	Benzene	250	15	2.14	0.49	3.07	19.56	3.36[b]	...	...	...	...	...	...	98
3	16.36	Benzene	250	10	2.27	0.57	3.24	20.48	3.48[b]	...	...	...	...	...	...	103
4	16.36[c]	Benzene	250	10	5.8	*d*	0	21.4	5.5	...	...	...	...	...	...	101
5	16.36[e]	Benzene	240	60	5.9	*d*	0	22.1	6.9	...	...	...	...	...	...	107
6	16.36	Toluene	250	15	2.15	0.50	2.88	19.13	1.31	CH_3	0.98	2.09[f]	1.04	H	*g*	106
7	16.36	Toluene	250	10	2.02	0.50	2.15	19.93	0.95	CH_3	0.72	1.38	0.78	H	0.18	98
8	16.36	Toluene	250	10	2.11	0.57	2.16	20.26	0.99	CH_3	0.72	1.54[f]	0.77	H	*g*	100
9	16.36	Cyclohexane[h]	250	10	5.0	*d*	2.4	20.2	0.6	...	0	0	0	...	...	96
10	49.08	*o*-Xylene	250	10	5.5	1.4	3.0[i]	61.2	5.2	1,2-$(CH_3)_2$	2.8[j]	6.4[k]	...	*o*-CH_3	1.5	99
11	49.08	*m*-Xylene	250	10	6.34	2.35	7.50	63.6	2.65	1,3-$(CH_3)_2$	0.87[l]	3.46[m]	3.75[n]	*m*-CH_3	0.2	105
12	49.08	*p*-Xylene	250	10	6.6	1.6	4.06[i]	61.5	3.9	1,4-$(CH_3)_2$	7.44[o]	...	...	*p*-CH_3	2.45	99
13	49.08	Mesitylene	250	10	6.1	1.5	5.1[i]	60.6	5.6	2,4,6-$(CH_3)_3$	2.7	...	...	3,5-$(CH_3)_2$	2.8	99
14	49.08	Nitrobenzene	230	10	11.9	1.6	1.50	61.1	2.8	NO_2	1.84	3.62	1.90	...	1.76[p]	96
15	49.08	Fluorobenzene	250	10	9.6	1.9	4.7[i]	55.4	2.7	F	1.13	4.19	2.45	...	...	93
16	49.08	Chlorobenzene	250	10	7.4	1.5	5.78[i]	29.3	29.6[q]	Cl	1.05	5.00	2.79	...	...	91
17	49.08	Anisole	250	10	7.8	1.7	1.0[i]	66.4	2.2	OCH_3	2.0	5.6[r]	1.2[r]	...	...	95
18	49.08	Cyclohexane[h]	250	10	13.06	1.0	14.4	50.4	1.66	...	...	...	...	*s*	0.02	99
19	2040	Diphenyl ether[t]	230	95	590	*d*	...	580	74	OC_6H_5	65	235	142	...	80[u]	94

[a] Approximately 5 ml./g. of cupric benzoate was used. [b] We were unable to distinguish between formation from attack on benzene or by decarboxylation of benzoylsalicylic acid. [c] 49 mmoles of CuO was added. [d] Included with salicylic acid. [e] 69 mmoles of CuO was added. [f] Includes a small amount of benzyl benzoate. [g] Included with *m*-tolyl benzoate. [h] For comparison with aromatic substrates. [i] Calculated from uncorrected peak area. [j] 2,3-Dimethylphenyl benzoate. [k] 3,4-Dimethylphenyl benzoate. [l] 2,6-Dimethylphenyl benzoate. [m] 2,4-Dimethylphenyl benzoate. [n] 3,5-Dimethylphenyl benzoate. [o] 2,5-Dimethylphenyl benzoate. [p] Benzanilide. [q] Derived in part by reaction with chlorobenzene. [r] Incomplete peak separation with v.p.c. analysis. [s] Cyclohexyl benzoate. [t] Air was bubbled through the reaction mixture for 85 min. at rate of 4000 cc./min. [u] Higher boiling material where two hydrogen atoms of diphenyl ether were replaced by the benzoyloxy group.

phatic carboxylic acid is used as the oxidizing agent, only the ester reaction is possible. This has been observed experimentally and this reaction will be discussed in a subsequent report. Therefore, flexibility in the desired predominant reaction can be realized by a proper choice of reaction systems: (1) protic solvents like water or benzoic acid for the phenol reaction; (2) aprotic aliphatic hydrocarbons for the salicylic reaction; and (3) cupric salts of aliphatic carboxylic acids in aprotic aromatic substrates for the ester reactions.

The distribution of isomers produced by the ester reaction with a variety of monosubstituted aromatic substrates is shown in Table II. The nature of the substituent appears to have only a slight effect on the orientation. Steric factors seem to play a more significant role. The *ortho* positions, which were hindered by the proximity of the substituent, were substituted only half as frequently as the *meta* positions. The ratios of *meta* to *para* substitution were approximately the statistical value.

TABLE II

DISTRIBUTION OF ISOMERS PRODUCED BY REACTION OF CUPRIC BENZOATE WITH MONOSUBSTITUTED AROMATIC SUBSTRATES

Substrate	*ortho*	*meta*	*para*
Anisole	1.00	2.80	0.60
Toluene	1.00	2.13	1.06
	1.00	1.92	1.08
	1.00	2.14	1.07
Nitrobenzene	1.00	1.97	1.03
Fluorobenzene	1.00	3.71	2.17
Chlorobenzene	1.00	4.76	2.66

The steric effect is also demonstrated by the isomer ratios found with the xylenes. The vacant positions of *o*-xylene are essentially equivalent by virtue of the directing effect of the methyl groups. Substitution occurred two to three times more frequently in the less hindered 4- and 5-positions than in the 3- and 6-positions. With *m*-xylene, the ratio of substitution for the 2-, the equivalent 4- and 6-, and the 5-positions was 1:4.0:4.3. This ratio appears to support a mechanism which would be influenced primarily by steric factors.

The amount of ester produced from mesitylene was only about one-third as large as that obtained from the xylenes. Fewer positions were available for substitution, however; the relatively severe degree of steric hindrance appears to be the most important factor. Furthermore, a considerable amount of attack had occurred on the exposed methyl groups to give 3,5-dimethylbenzyl benzoate.

This result emphasized that aromatic substrates such as toluene or the xylenes possess both aliphatic and aromatic hydrogens for replacement reactions. Early work with these materials indicated that attack had occurred exclusively on the aromatic hydrogen atoms. However, it was eventually proved that benzyl esters, resulting from the displacement of a methyl hydrogen, were also produced in small quantities, with all aromatic substrates containing a methyl group. They simply were not easily detected by the ordinary distillation and preparative v.p.c. techniques used to separate and identify the reaction products. With *p*-xylene, however, where only one xylyl benzoate ester was predicted, a small but well-isolated peak was present on the vapor phase chromatogram. This was identified as *p*-methylbenzyl benzoate (run 12). With the appearance of this product, a more careful investigation of the ester product fractions of other runs, where aliphatic hydrocarbon groups were present on the aromatic substrate, was required. Authentic samples of the benzyl ester were first mixed with a portion of the reaction product mixture to determine the particular v.p.c. fraction (usually an isomeric phenyl benzoate derivative) where it appeared as a minor product. When it was impossible to make a separation, an estimate of the relative amounts was made from the area of the peak characteristic of the methylene group in the n.m.r. spectra.

The reaction carried out in chlorobenzene produced an abnormally large amount of phenyl benzoate. This occurred by displacement of chlorine by the acyloxy group. This is *not* an oxidation–reduction reaction and is not dependent on the oxidizing power of the copper(II) salt. The details of this reaction will be discussed in a subsequent paper.

Discussion

The precise manner in which the copper(II) functions as the oxidizing agent in reactions involving cupric salts of carboxylic acids has been a matter of considerable interest in this series of papers. We have hesitated to show a preference between a heterolytic or homolytic process. The stoichiometry requires a two-electron oxidation–reduction process.

A heterolytic process, favored by Toland,[7] has been used to explain the oxidative attack at a position *ortho* to the carboxyl group.[7,8] The reduction of cupric ion to copper metal in the primary step is required. Failure actually to detect copper as a reaction product was rationalized by postulating a rapid subsequent reaction with cupric salt to produce the cuprous salt.[8]

Early support for a heterolytic process in this laboratory was based chiefly on the observation that the reaction for the oxidation of benzoic acid to phenol was not affected significantly by a great variety of metal ions or by certain organic compounds noted for their ability to poison free-radical reactions. The fact that phenol was a reaction product and was always present in the system would, at first glance, seem to preclude the possibility of an "ordinary" free-radical mechanism. However, it has been demonstrated that there is a great variety of homolytic reactions, some of which may occur even in highly ionizing solvents such as water.[9]

Schoo and co-workers[10] favor a homolytic mechanism for the phenol reaction. This suggests two single-electron oxidations by a pair of cupric ions. In this event, copper metal would never be formed.

We have observed that the copper(I) salt is the reduction product isolated in an overwhelming majority of cases for the various reactions discussed in this series. Furthermore, added copper metal, in the absence of oxygen, does not appear to dissolve in (or is it

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(7) W. G. Toland, *J. Am. Chem. Soc.*, **83**, 2507 (1961).

(8) W. W. Kaeding, *J. Org. Chem.*, **26**, 3144 (1961).

(9) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, Chapter 2.

(10) W. Schoo, J. V. Veenland, J. C. Van Velzen, T. J. DeBoer, and F. L. J. Sixma, *Rec. trav. chim.*, **82**, 959 (1963).

deposited from) a solution of cupric benzoate in benzoic acid heated for periods of many hours at temperatures up to 250°.[11]

A variety of single-electron oxidations of phenols by metal ions, including copper(II),[12] has been observed.[13,14] The facile interconversion of copper(I) and (II) salts has been an integral part of the mechanism of the peroxy ester reaction, recently reviewed by Sosnovsky and Lawesson.[15] A similar type of single-electron transfer reaction has also been used to explain the copper-catalyzed Sandmeyer and Meerwein reactions.[16]

The ester reaction appears to be unique in this series because oxidation occurs at all available positions on the aromatic ring. The products isolated and distribution of isomers suggest an attack by the benzoyloxy radical. The generation of benzoyloxy radicals from benzoyl peroxide and their subsequent reaction with various aromatic substrates has been extensively investigated.[17-19] Spontaneous decarboxylation of the benzoyloxy radical predominates in aromatic aprotic solvents. The phenyl radical which is produced subsequently reacts with the solvent to give a biphenyl derivative. By contrast, when benzoyl peroxides were heated with phenols, a reaction occurred with the latter before decarboxylation to give primarily *ortho*-substituted benzoyloxyphenols.[20] A bimolecular, four-center process was proposed by the authors; however, the presence of a radical complex which significantly modified the expected reactions was also suggested. The aromatic substrates shown in Table I resemble phenols in their reactivity toward a benzoyloxy radical, since the final product is an ester.

A comparison of the isomer ratios of phenyl derivatives which Daunley and Zarensky[21] obtained by a reaction of benzoyl peroxide with toluene and the benzoyloxy derivatives obtained with run 7, Table I, is shown in Table III. The distribution of isomers does not suggest a close relation between the reactions.

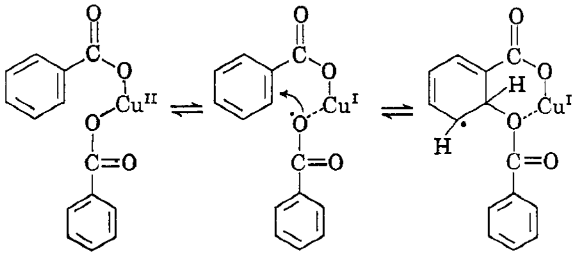
A homolytic mechanism for the various reaction paths of cupric benzoate, shown by eq. 8 to 11, is proposed. It involves a pair of single-electron changes for the oxidation–reduction reaction with cupric ion and is consistent with the reaction products isolated. The ability of copper(II) to accept an electron and the steric position of the benzoate ions with relation to the cupric ion are key features. A radical complex or a highly concerted mechanism is suggested to account for the observed stability toward decarboxylation.

TABLE III

COMPARISON OF ISOMER DISTRIBUTION OF REACTION PRODUCTS OF TOLUENE WITH BENZOYL PEROXIDE AND CUPRIC BENZOATE

Isomer	With $(BzO)_2$,[a] %	With $Cu(OBz)_2$,[b] %
Benzyl	15	6
ortho	65	24
meta	19	45
para	16	25

[a] Reference 21, at 75°. Hydrogen was replaced by a phenyl group to give a hydrocarbon. [b] Run 7, Table I, at 250°. Hydrogen was replaced with the benzoyloxy group to give an ester.



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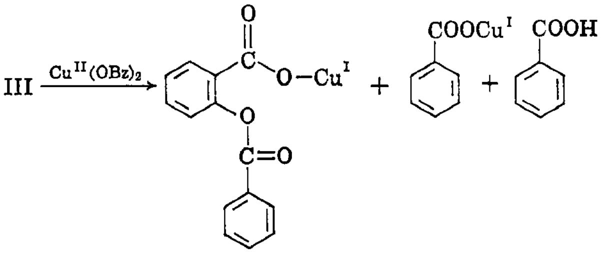

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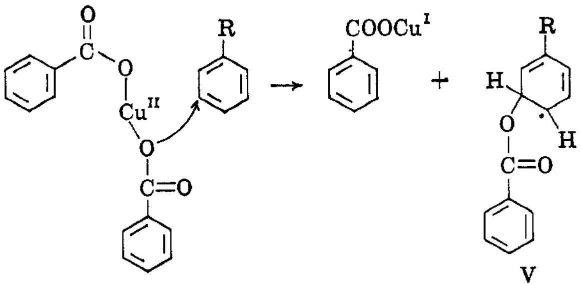

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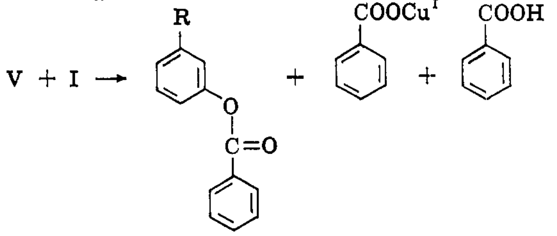

(11)

The orientation of the cupric benzoate molecule just prior to reaction for the phenol and salicylic reactions is shown by eq. 8. When the copper(II) begins to accept an electron from the oxygen atom, it starts to generate a benzoyloxy radical. The oxygen with radical character (II) is in a favorable position to attack only the *ortho* positions.

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[11] The most clearly demonstrated case where copper metal appeared as a reaction product was observed when water was used as the solvent.[8] However, the initial production of cuprous sulfate was postulated. Cuprous benzoate is rapidly hydrolyzed when the concentration of free acid is low. The cuprous oxide formed has a color very similar to that of finely divided

$$2CuOBz + H_2O \rightleftharpoons Cu_2O + 2HOBz$$

copper metal. Analysis for copper content alone would make it difficult to distinguish it from the metal slightly contaminated with organic material. We have been able to identify positively the form of copper by means of X-ray diffraction patterns which are distinctive for the various possible crystalline compounds. Usually, Cu_2O is the species responsible for the dull copper color.

[12] W. W. Kaeding, *J. Org. Chem.*, **28**, 1063 (1963).

[13] K. U. Ingold, *Chem. Rev.*, **61**, 563 (1961).

[14] M. S. Kharasch and B. S. Joshi, *J. Org. Chem.*, **22**, 1439 (1957).

[15] G. Sosnovsky and S. O. Lawesson, *Angew. Chem. Intern. Ed. Engl.*, **3**, 269 (1964).

[16] J. K. Kochi, *J. Am. Chem. Soc.*, **79**, 2942 (1957).

[17] Reference 9, p. 484.

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The intermediate cuprous salt radical III is then oxidized by a second molecule of cupric benzoate to give *o*-benzoyloxybenzoic acid (IV) (eq. 9). In protic solvents, decarboxylation occurs to give phenyl benzoate (phenol reaction) as the major product. In aprotic solvents, the salicylic reaction predominates.

When cupric benzoate is oriented in configuration Ia, the incipient benzoyloxy radical is in a position to attack a solvent molecule to produce a cyclohexadienyl intermediate radical V, analogous to III (eq. 10). This sequence is the ester reaction. In this case, the reacting components are not held in a rigid configuration with respect to each other and attack would be expected at any vacant position of the aromatic ring of the solvent.[22] The amount of *ortho* isomer produced would be influenced primarily by the size of the R group of the solvent. The final ester product which is isolated is produced by a subsequent oxidation with the second mole of cupric benzoate (eq. 11).

According to this mechanism, the most labile hydrogen atom of the intermediate radical, III or V, is the one attached to the carbon atom containing the benzoyloxy group. This is the atom which is oxidized by the second mole of cupric benzoate. An exchange between III and deuterium oxide would account for the exclusive *ortho* deuteration observed by Schoo and co-workers.[23]

Experimental Section

Approximately 25 g. of aromatic substrate and 5.0 g. of cupric benzoate[24] were sealed in glass bombs, under vacuum, and heated in a Parr high-pressure hydrogenation apparatus for the prescribed period of time. Some of the substrate was placed in the metal bomb to equalize the pressure on the walls of the glass bomb.

The contents of from one to three identical bombs were poured on a weighed, sintered-glass filter and rinsed with dry ether. The insoluble portion was a mixture of cuprous benzoate, cuprous salicylate, and cuprous oxide. The latter was identified by the appearance of characteristic bands in the powder X-ray diffraction pattern.

Authentic samples of cuprous benzoate and cuprous salicylate were prepared by reduction of the corresponding cupric salts with boiling phenol, in a nitrogen atmosphere. The infrared spectra of the ether-insoluble portion was characteristic of cuprous benzoate contaminated with cuprous salicylate.

Anal. Calcd. for $C_7H_5CuO_2$: Cu, 34.4. Calcd. for $C_7H_5CuO_3$: Cu, 31.7. Calcd. for Cu_2O: Cu, 88.8. Found: Cu, 34.4 (run 6), 36.0 (run 9), 35.4 (run 10), 36.1 (run 15), 32.4 (run 17).

This cuprous salt mixture was treated with ether saturated with dry HCl to release and extract the organic acids. Most of the salicylic acid was present in this mixture.

The original filtrate was diluted to 250 ml. with ether. A 50-ml. aliquot was heated to 100° at 20 mm. pressure to remove volatile components and was set aside for analysis. A 200-ml. aliquot was extracted with 10–15 ml. of dilute HCl to decompose and remove a trace of soluble copper salts. The solution was then extracted with saturated aqueous bicarbonate solution to remove the soluble acids, primarily benzoic acid with some *o*-benzoyloxybenzoic acid. The latter was identified by distinctive, isolated peaks in the infrared spectra.[5] The aromatic acids were recovered by acidification and extraction with methylene chloride followed by distillation of the solvent. Evaporation of the ether solution produced the neutral fraction. This treatment did not appear to hydrolyze any of the benzoic anhydride.

Salicylic acid and benzoylsalicylic acid, mixed with benzoic acid, were titrated with bromine by the well-known method[25] used for the determination of phenols. Three equivalents of bromine per mole of salicylic and *o*-benzoyloxybenzoic acids was used to give tribromophenol and CO_2.

The neutral fraction was separated into the various components and analyzed by v.p.c. techniques. Aerograph Model A90-P-2 and HyFy instruments, manufactured by Wilkins Instrument Co., were used. The structure of all esters was verified by a comparison of physical properties or infrared spectra with an authentic sample.

The benzyl-type esters were identified in a similar manner when possible. When the amount was extremely small, a retention time identical with an authentic sample was used for identification. When a complete physical separation from an isomeric phenyl benzoate type ester was unsuccessful with the preparative v.p.c., the (two-component) mixture was analyzed by means of n.m.r. spectra. The integrated peak area in the 5.3–5.4 p.p.m. region, characteristic of the methylene group, was used to confirm the presence and estimate the amount of the benzyl ester.

Authentic samples of the compounds found in the neutral fraction were used to prepare standards to determine the relation between the mole fraction and the peak area of the v.p.c. spectrogram.

The techniques for the utilization of air as the oxidizing agent (run 19) have been described in the previous paper of this series.[5]

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[22] Only attack at the *meta* position is shown in eq. 10.

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